of Alzheimer's and Parkinson's disease. Clinical trials should be performed for herbal extracts, which showed neuroprotective activity in vitro. Also herbal extracts without proved activity in this field should be investigated.

268. ANTIOXIDANT DEFENCES AND OXIDATIVE STRESS IN ELDERLY ALZHEIMER PATIENTS

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Oxidation has been proposed to be an important factor in the pathogenesis of Alzheimer's disease (AD).

Objective is to investigate markers of oxidation and antioxidants {vitamin A: Retinol.(R-OH) and E: alpha-tocoferol (T-OH)] in normally elderly people with AD. Subjects: Fourteen patients with AD and fourteen elderly control (C), not undergoing any treatment known to have a strong influence on oxidative stress or antioxidant defence systems. The investigation conforms the principles outlined in the declaration of Helsinki. Methods: measured serum level of R-OH and T-OH by High-Performance liquid chromatography (HPLC) and lipid peroxidation (Malondialdehyde: MDA) and lipids (Total Cholestrol: TC and Triglycerides:TG) by colorimetric methods and spectrophotometric detection. Results: The two groups were similar in age. The mean concentration of MDA was higher in AD (4,11±1.11 Vs 1.53±0.69) µmol/l, p≤0.05. The R-OH (1.54±0.45 Vs 2.4±0.89)µM/l and T-OH (8.41±03.64 Vs 25.84±8.22))µM/l were lower in those AD than in C subjects (p≤.05). After adjusment for lipids (TC+TG) the vitamin E was even lower in AD (7.78±3.05 Vs 27.67±7.34))µM/l, (p≤0.05). Conclusion: Higher levels of peroxidation products (MDA) reflect the presence of oxidative stress in AD patients and lower of R-OH and T-OH with AD than C could suggest that those antioxidant vitamins have been consumed as a result of excessive production of free radicals.

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269. DRUG INTERACTIONS BETWEEN LAMOTRIGINE AND PSYCHOACTIVE DRUGS: EVIDENCE FROM A THERAPEUTIC DRUG MONITORING SERVICE

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We present a study on the pharmacokinetic interaction potential of lamotrigine with focus on psychoactive drugs, based upon routine serum concentration measurements performed in our laboratory. In total, 1733 serum samles of lamotrigine from 829 patients were included. The median lamotrigine concentration-to-dose ratio (LTG-CDR) was 58 (interquartile range 39–96) (nmol/L)/(mg/d). A linear mixed model was used to indentify and quantitate the effect of factors influencing the LTG-CDR. In addition to age and gender, a total of 35 different comedications (25 drugs used in psychiatry as well as 10 other drugs) were evaluated. With females <70 years of age as the reference group, factors found to lower the LTG-CDR significantly were male gender (−14%) and co-treatment with carbamazepine (−42%), ethinylestradiol (−27%), fluoxetine (−36%), lithium (−14%), phenytoin (−57%), phenobarbital (−28%) and topiramate (−25%). Factors associated with a significantly higher LTG-CDR were age above 70 years (+34%) and co-treatment with valproate (+191%). No other antidepressants than fluoxetine and none of the antipsychotics or benzodiazepines studied were associated with an altered LTG-CDR. Concerning pharmacokinetic drug interactions, we conclude that lamotrigine can be safely combined with most psychotropic drugs.

270. THE EFFECT OF SOME CENTRAL ACTIVE SEROTONERGIC AGONISTS AND ANTAGONISTS ON THE SOMATOSENSORY EVOKED RESPONSES IN URETHANE ANAESTHETIZED RAT

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In this study, we investigated the effects of some serotonergic drugs on the somatosensory evoked responses. Evoked responses were recorded from the sensory-motor cortex in urethane-anaesthetized rat. The intraperitoneal administration of the serotonin precursor, 5-hydroxytryptophan (5-HTP), produced a marked depressant effect on the mass evoked responses. This was manifested by a significant increase in the latency and decrease in both the positive and negative waves. Conversely, selective 5-HT3 blockers, MDL72222 and GR383032F, produced a reduction in the latency and an increase in the amplitudes of the initial positive and negative waves of evoked responses. The agonist of serotonin, 5- methoxytryptamine (5-MEOT), and the depletory of 5-hydroxytryptamine, parachlorophenylalanine (p-CPA), induced an increase in the latency and reduced amplitude of evoked responses. This study provides further evidence that serotonin modulate the depth of anesthesia which is reflected through the changes of parameters of the evoked responses.

271. EFFECTS OF TAMOXIFEN ON MORPHOLOGICAL AND ULTRASTRUCTURAL ASPECTS IN THE DEVELOPING HIPPOCAMPUS OF RAT

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Maternal steroids modulate various functions in the brain. However tamoxifen treatment induced cell death in the hippocampus formation of the prenatal and postnatal rat. To test the role of estradiol on hippocampus developing during prenatal and postnatal, animals at full term received four doses of the estrogen-receptor low-efficacy partial agonist tamoxifen and their brain were removed, 6 hours after the last injection. We undertook this study on rat with tamoxifen to investigate the density of cell in various regions as CA1, CA3, DG and subiculum. The novel finding in this study is the different in density of cell in the various stages of developing. Also our results show that tamoxifen treatment at full female rat significantly lowered the numbers in CA1. These finding provide histochemical and ultrastructural evidence for neuroprotective effects of estrogen.

478. USE OF MARGARINE ENRICHED IN PHYTOSTEROLS BY PATIENTS AT HIGH CARDIOVASCULAR RISK

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Background: Little is known about the use of phytosterol-containing margarines in patients at cardiovascular (CV) risk. We determined the proportion of users of margarine in a population at high cardiovascular risk, and their characteristics. In addition, the correlates of effective use (use at effective doses) were identified.

Methods: Patients with at least two cardiovascular risk factors in addition to dyslipidemia (primary prevention) or with past cardiovascular disease (secondary prevention) were recruited by GPs. Baseline characteristics were collected from a computerized GP database linked to a survey. GPs recorded patterns of use of margarine. First, users were compared to non-users. Then, analyses were conducted to identify characteristics of 'effective' users (>250 mg over 3 days).

Results: Among 1622 patients with documented margarine consumption, a minority used margarine (14.8%), and only 5.4% of